International Research Journal of Pharmaceutical and Applied Sciences (IRJPAS)
Available online at **www.irjpas.com**
Int. Res J Pharm. App Sci., 2013; 3(6):35-38

Research Article

DEVELOPING PLATFORM TECHNOLOGY FOR FLOATING TABLETS

K. P. R. Chowdary*, K.Ravi Shankar and CH.K.L.Chaitanya
Vikas Institute of Pharmaceutical Sciences,Nidigatla Road, Rajahmundry- 533103
*Corresponding Author: Prof. K. P. R. Chowdary; Email: prof.kprchowdary@rediffmail.com

Abstract: The principle of floating tablets offers a simple and practical approach to achieve increased residence time in the stomach and upper G.I. tract to enhance the bioavailability and to obtain controlled release. Floating tablets are designed based on gas generating principle. Design of floating tablets needs a strong matrix forming polymer.Floating enhancers such as beeswax and ethyl cellulose are also needed along with the matrix forming polymer to reduce floating lag time and to achieve floating over longer period of time.The objective of the present study is to develop and evaluate a platform technology based on the use of 50 % matrix forming polymer, 5% bees wax and 5% ethyl cellulose for the design of floating tablets of a highly water soluble drug, diltiazem hydrochloride.Matrix tablets each containing 90 mg of diltiazem were prepared employing (i) HPMC K100M (ii) sodium CMC (iii) sodium alginate and (iv) methyl cellulose each at 50 % concentration, sodium bicarbonate(12%) as gas generating agent, ethyl cellulose (5%) and bees wax (5%) as floating enhancers and evaluated. The floating tablets prepared based on the proposed platform technology employing HPMC K100 M, sodium CMC and sodium alginate as matrix formers were of good quality with regard to drug content, hardness and friability. In the invitro buoyancy study, the floating lag time of various tablets was in the range 7-25 seconds. Floating time was in the range 20-24 hours with the floating tablets formulated employing HPMC K100 M, sodium CMC and sodium alginate.Diltiazem release from the floating tablets prepared was slow and spread over 8-10 h and depended on the polymer used. Among all sodium CMC gave relatively slow release of diltiazem over 10 h. Drug release from the floating tablets prepared was diffusion controlled and mechanism of release was by non-fickian (anomalous) diffusion.The platform technology based on the use of 50 % matrix forming polymer, 5 % bees wax and 5% ethyl cellulose was suitable for the design of floating tablets of water soluble drug, diltiazem hydrochloride.

Key words: Floating tablets, Diltiazem hydrochloride, HPMC K 100 M, Sodium CMC,Sodium Alginate, Methyl Cellulose, Platform Technology

INTRODUCTION

Oral drug delivery is the most desirable and preferred method of administering therapeutic agents for their systemic effects. The high level of patient compliance in taking oral dosage forms is due to the ease of administration, patient compliance, flexibility in formulation and handling of these forms[1]. However the oral route of administration suffers with certain drawbacks mainly short residence time of the dosage form in the GI tract, unpredictable gastric emptying, degradation of the drug due to highly reactive nature of GI contents and existence of an absorption window in the gastric and upper small intestine for several drugs[2,3]. Gastric emptying is a complex process and makes *in vivo* performance of the drug delivery system uncertain. Formulation of floating drug delivery systems is an useful approach to avoid this variability with increased gastric retention time of the drug delivery system. Floating systems or hydrodynamically controlled systems are low-density systems that have sufficient buoyancy to float over the gastric contents and remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time .While the system is floating on the gastric contents, the drug is released slowly at the desired rate from the system. After release of drug, the residual system is emptied from the stomach .This results in an increased gastric residence time and a better control of the fluctuation in plasma drug concentration [4, 5].

Several approaches are currently used to retain the dosage in the stomach. These include bioadhesive systems[6],swelling and expanding systems[7,8],floating systems[9,10] and other delayed gastric emptying devices[11,12] .

The principle of floating tablets offers a simple and practical approach to achieve increased residence time in the stomach and upper G.I. tract to enhance the bioavailability and to obtain controlled release. Floating tablets are designed based on gas generating principle. Design of floating tablets needs a strong matrix forming polymer. Several polymers such as various viscosity grades of HPMC, Carbopol 934P, Eudragit RL, calcium alginate,Chitosan, Xanthan gum, guargum, ethylcellulose etc., have been used in the design of floating tablets of various APIs. Preliminary studies indicated that floating enhancers such as bees wax (5%) and ethyl cellulose (5 %) are also needed along with the matrix forming polymer to reduce floating lag time and to achieve floating over longer period of time.

The objective of the present study is to develop a platform technology based on the use of 50 % matrix forming polymer, 5% bees wax and 5% ethyl cellulose for the design of floating tablets. The technology was evaluated using diltiazemHCl (a water soluble drug) as a model drug for gastro retentive floating tablets. Four different polymers namely HPMC K 100 M, sodium CMC, sodium alginate and

methyl cellulose were evaluated as matrix forming polymers for floating tablets.

Diltiazem hydrochloride is calcium channel blocker used as anti-hypertensive and anti-anginal drug. It has poor bioavailability (30-50%) and has absorption window in upper part of the GI tract[13]. It has short biological half-life of about 3.5 hours and is rapidly eliminated. Floating tablets of diltiazem were designed in the present study to enhance its bioavailability and to achieve controlled release over 10-12 hours for b.i.d administration.

EXPERIMENTAL

Materials

Diltiazem was a gift sample from M/s Micro Labs Ltd, Pondicherry. Hydroxy propyl Methyl Cellulose K 100M, sodium CMC (high viscosity,500-600 cps), sodium alginate, methyl cellulose (4000 cps), ethyl cellulose, sodium bicarbonate and beeswax were procured from commercial sources. All other materials used were of Pharmacopoeial grade.

Methods

Preparation of Floating Tablets

Matrix tablets each containing 90 mg of diltiazem were formulated employing (i) HPMC K100M (ii) sodium CMC (iii) sodium alginate and (iv) methyl cellulose each at 50 % concentration in theformula. Sodium bicarbonate was used as gas generating agent at 12%, strength in each case. Bess wax and ethyl cellulose were used as floating enhancer each at 5%concentration in all the formulations. The tablets were prepared by melt granulation method as per the formula given in Table1.

The required quantities of diltiazem, HPMC K100M / sodium CMC/ sodium alginate/ methyl cellulose, ethyl cellulose andsodium bicarbonate were thoroughly mixed in a dry mortar by following geometric dilution technique. Beeswax was melted in a dry beaker and the blend of the above mentioned ingredients was added to the molten beeswax and mixed to form granular aggregates. The granules formed were passed through mesh No. 16 to break the aggregates. The lubricants talc and magnesium stearate were passed through mesh No. 60 on to the dry granules and blended in a closed polyethylene bag. The tablet granules were compressed into tablets on a 8-station tablet punching machine (Karnavathi RimekMinipress II) to a hardness of 4-5 Kg/cm^2.

Evaluation of Tablets

Hardness of the tablets was tested using a Monsanto hardness tester. Friability of the tablets was determined in a Roche friabilator. Disintegration time of the tablets was determined using a Paramount tablet disintegration test machine using water, 0.1N HCl and phosphate buffer of pH7.4 as the test fluids.

Estimation of Diltiazem

An ultraviolet (UV) spectrophotometric method based on the measurement of absorbance at 237 nm in 0.1N hydrochloric acid was used for the estimation of diltiazem. The method obeyed Beer-Lambert's law in the concentration range of 0-10µm/mL. When a standard drug solution was assayed repeatedly (n=6), the relative error (accuracy) and coefficient of variation (precision) were found to be 0.85% and 1.60%, respectively. No interference from the excipients used was observed.

Floating Lag Time and Floating Time

In Vitro buoyancy was determined by measuring floating lag time and duration of floating. The tablets were placed in a 250 ml glass beaker containing 0.1N HCl. The time required for the tablet to rise to the surface and float was determined as floating lag time. The duration in which the tablet remains floating was determined as floating time.

Drug Release Study

Drug release from the floating tablets prepared was studied using 8-station dissolution rate test apparatus (Labindia, DS 8000) employing a paddle stirrer at 50 rpm and at a temperature of 37 ± 1^0C. Hydrochloric acid, 0.1N (900 mL) was used as dissolution fluid. A 5mL aliquot ofdissolution medium was withdrawn through a filter (0.45µm) at different time intervals and assayed spectrophotometrically by measuring absorbance at 237 nm. All drug release experiments were conducted in triplicate (n=3).

Data Analysis

Drug release data were analysed as per Zero order, first order. Higuichi[14] and Korsemeyer - Peppas[15] equation models to assess drug release kinetics and mechanism from the floating tablets.

RESULTS AND DISCUSSION

The principle of floating tablets offers a simple and practical approach to achieve increased residence time in the stomach and upper G.I. tract to enhance the bioavailability and to obtain controlled release. Floating tablets are designed based on gas generating principle. Design of floating tablets needs a strong matrix forming polymer.Preliminary studies indicated that floating enhancers such as beeswax and ethyl cellulose are also needed along with the matrix forming polymer to reduce floating lag time and to achieve floating over longer period of time.The objective of the present study is to develop and evaluate a platform technology based on the use of 50 % matrix forming polymer, 5 % bees wax and 5% ethyl cellulose for the design of floating tablets.

Matrix tablets each containing 90 mg of diltiazem were prepared employing (i) HPMC K100M (ii) sodium CMC (iii) sodium alginate and (iv) methyl cellulose each at 50 % concentration, sodium bicarbonate(12 %) as gas generating agent, ethyl cellulose (5%) and bees wax (5%) as floating enhancers and evaluated with an objective to develop a platform technology for the design of floating tablets.

Table 1.Formulae of Floating Tablets of Diltiazem Prepared by Melt Granulation Method Employing the Proposed Platform Technology

S. NO	Ingredient (mg/tablet)	Formulation			
		F1	F2	F3	F4
1	Diltiazem HCl	90	90	90	90
2	HPMC K100M	175	-	-	-
3	Sodium CMC	-	175	-	-
4	Sodium alginate	-	-	175	-
5	Methyl cellulose	-	-	-	175
6	Sodium bicarbonate	42.0	42.0	42.0	42.0
7	Ethyl cellulose	17.5	17.5	17.5	17.5
8	White beeswax	17.5	17.5	17.5	17.5
9	Talc	4.0	4.0	4.0	4.0
10	Magnesium stearate	4.0	4.0	4.0	4.0
	Total weight(mg)	350	350	350	350

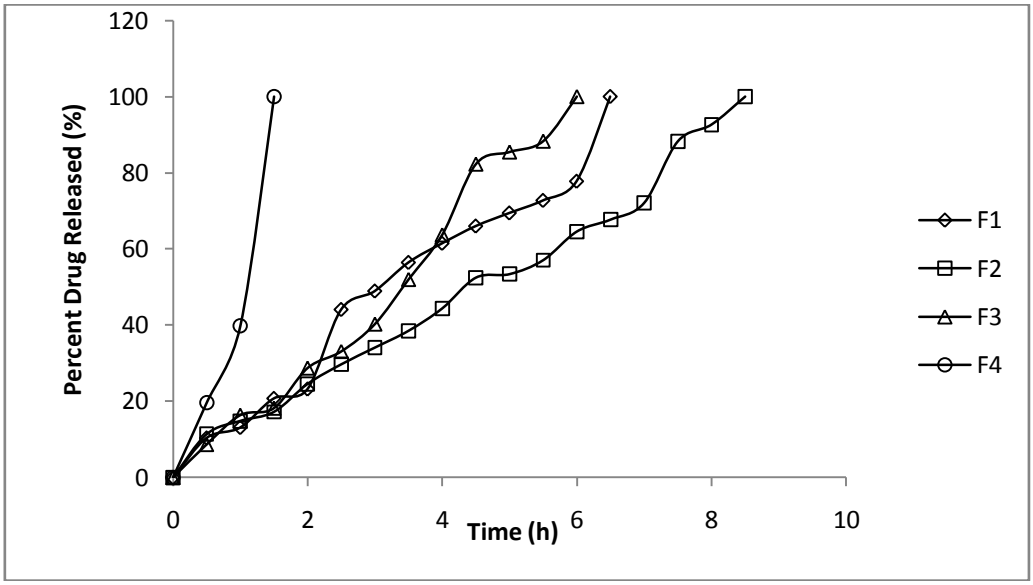

Fig .1: Drug Release Profiles of Floating Tablets of Diltiazem Prepared by Melt Granulation Method Employing the Proposed Platform Technology (F1: HPMC K 100 M, F2: Sodium CMC, F3: Sodium Alginate, F4: Methyl Cellulose)

Table 2. Dissolution Parameters of Floating Tablets of Diltiazem Prepared by Melt Granulation Method Employing the Proposed Platform Technology

Formulation	T_{50} (h)	T_{90} (h)	Dissolution Rate		Release Exponent (n)
			K_0 (mg/h)	$K_1(h^{-1})$	
F1	3.2	6.3	13.88	0.256	0.93
F2	4.4	7.8	10.81	0.254	0.806
F3	3.5	5.6	17.43	0.402	1.005
F4	1.1	1.4	80.39	0.508	----

Hardness of the tablets was in the range 7-8 Kg/cm^2.Weight loss in the friability test was less than 0.85% in all the cases. All the tablets prepared contained diltiazem hydrochloride within 100±3% of the labelled claim. Tablets prepared employing HPMC K100 M, sodium CMC and sodium alginatewere found to be non-disintegrating in water and aqueous acidic (pH 1.2) and alkaline (pH7.4) fluids.Tablets formulated employing methyl cellulose disintegrated in 30-60 min As such the prepared tablets with HPMC K100 M, sodium CMC and sodium alginatewere of good quality with regard to drug content, hardness and friability. In the *invitro* buoyancy study, the floating lag time of various tablets was in the range 7-25 seconds. Floating time was in the range 20-24 hours with the floating tablets formulated employing HPMC K100 M, sodium CMC and sodium alginate. Tablets formulated employing methyl cellulose disintegrated in 30-60 min in the *invitro* buoyancy test.

Diltiazem release from the floating tablets formulated was studied in 0.1N hydrochloric acid. Diltiazem release from the floating tablets prepared was slow and spread over 8-10 h and depended on the polymer used. The release data were analysed as per zero order, first order, Higuchi and Korsemeyer- Peppas kinetic models. Diltiazem release parameters of the floating tablets

formulated are summarized in Table-2. The release data obeyed all the kinetic models tested with correlation coefficient (r) values above 0.902. Drug release from the floating tablets prepared was diffusion controlled as indicated by the linear Higuchi plots with correlation coefficient (r) greater than 0.937. When the release data were analysed as per Korsemeyer- Peppas equation, the release exponent 'n' was found to be in the range 0.806 – 1.02 indicating 'non-Fickian diffusion' as the release mechanism from the floating tablets prepared.Among all sodium CMC (50 %) along with ethyl cellulose (5%) and beeswax (5 %) was found to be the best matrix forming polymer for the design of floating tablets.

The results of the study indicated that the platform technology based on the use of
50 % matrix forming polymer, 5% bees wax and 5% ethyl cellulose was suitable for the design of floating tablets of water soluble drug, diltiazem hydrochloride.

CONCLUSIONS

1. The floating tablets prepared based on the proposed platform technology employing HPMC K100 M, sodium CMC and sodium alginate as matrix formers were of good quality with regard to drug content, hardness and friability.
2. In the *invitro* buoyancy study, the floating lag time of various tablets was in the range 7-25 seconds. Floating time was in the range 20-24 hours with the floating tablets formulated employing HPMC K100 M, sodium CMC and sodium alginate.
3. Diltiazem release from the floating tablets prepared was slow and spread over 8-10 h and depended on the polymer used. Among all sodium CMC gave relatively slow release of diltiazem over 10 h.
4. Drug release from the floating tablets prepared was diffusion controlled and mechanism of release was by non-fickian (anamolous) diffusion.
5. The platform technology based on the use of 50 % matrix forming polymer, 5 % bees wax and 5% ethyl cellulose was suitable for the design of floating tablets of water soluble drug, diltiazem hydrochloride.

REFERENCES

1. Ansel HC, Allen LV, Popovich NG. Pharmaceutical Dosage Forms and Drug Delivery Systems. Philadelphia, Lippincott Williams and Wilkins Chapter -3, **2003**: 23-31.
2. Agyilirah, G.A., Green,M.and Ducret,R., *Int.J.Pharm*, **1991**; 75: 241,.
3. Hoffman, A.F, Pressman, J.H. and Code CF, *Drug Dev. Ind.Pharm*, **1983**; 9: 1077.
4. Mayavanshi AV, Gajar SS. Floating drug delivery system to increase gastric retention of drug: A Review. J. Pharm. Res, **2008**; 1940: 345-348.
5. Vachhanisavan R, Patel Dipen, Prajapati ST, Patel CN. *J Chem. Pharma Res*, **2010**; 2(2): 57-64.
6. Santus, G., Lazzarini, G. and Bottoni.G.,Eur. J. Pharm. Bioparm., **1997**; 44: 39.
7. Deshpande, A.A, Rhodes, C.T., Shah, N.H. and Malick, A.W. *Drug Dev. Ind. Pharma*, **1996**; 22: 531.
8. Deshpande AA, Shah, NH, Rhodes CT and Malick W. *Pharma. Res*, 1997; 14: 815.
9. Menon, A., Ritshel, W.A. and Sakr,A. *J. Pharm. Sci*. **1994**; 83: 239,.
10. Whitehead L, Fell J, Collett JH, Sharma HL and Smith AM. *J.Control Release*, 1998; 55: 3.
11. Singh B and Kim K. *J. Control Release*, **2000**; 63: 235.
12. Chawla, G. and Bansal, A., *Pharm.Tech*, **2003**; 27: 50.
13. Kinney E, Moskovitz RM, Zelis RF. *J ClinPharmacol*, **1981**; 21: 337.
14. Higuichi T. *J .Pharm. Sci*, **1963**; 52: 1145.
15. Korsmeyer RW, Gurny R, Doelkar E, Buri P, Peppas NA. *Int. J .Pharm*, **1983**; 15: 25.